

## REMARKS

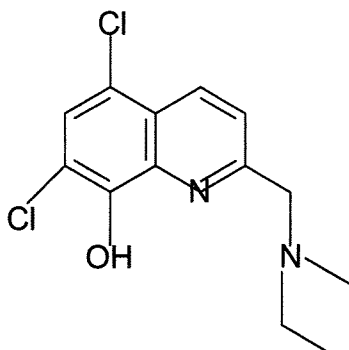
The Office Action has allowed Claims 30-36, 38 and 40. Specifically, the Office Action states that the rejections of Claims 32 and 33 under 35 U.S.C. §§102 and 103 are withdrawn due to Applicants amendments and the submitted Declaration showing unexpected results.

However, the Office Action has rejected Claims 37, 39 and 41 under 35 U.S.C. §112, first paragraph, as allegedly non-enabling.

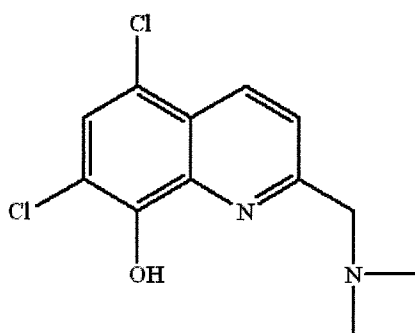
Applicants have herein cancelled certain claims, and are submitting a Supplemental Declaration, which when considered with the comments herein, are deemed to place the present case in condition for allowance. Favorable consideration is respectfully requested.

Specifically, Applicants have cancelled, without prejudice, Claims 37, 39 and 41 of the instant application. Applicants, however, have not abandoned the subject matter recited therein and reserve the right to file a continuation application directed to the cancelled subject matter.

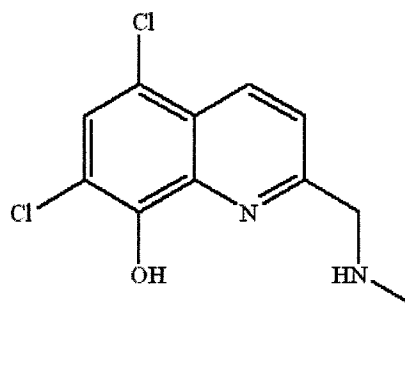
Applicants are also submitting herewith a second Declaration of Dr. Robert Cherny ("second Declaration") to present additional information which Applicants believe is relevant to the examination of the present application. Applicants respectfully submit that the testimony proffered in the second Declaration further supports the patentability of the allowed Claims, consistently with the testimony provided by the previous Declaration, dated September 16, 2008 ("previous Declaration"). Notably, the second Declaration presents additional data evidencing patentability not provided in the previous Declaration which Applicants wish to make of record. For example, the second Declaration includes a contemporaneous side by side comparison of the ionophore properties of the prior art compound disclosed in U.S. Patent No. 3,682,927 to Carissimi et al. ("Carissimi et al.") of the formula:



(the "CC compound"), with the ionophore properties of present compounds PBT 1033 and PBT 1051, having the structures:



PBT 1033



PBT 1051

designated "1033" and "1051", respectively.

The CC compound was defined in the previous Office Action by the Examiner as the closest prior art compound to the subject matter recited in allowed Claims 32 and 33.

The testimony in the second Declaration particularly elucidates the fact that the data presented in the first Declaration with respect to the CC compound was conducted at a different time than the data presented with respect to 1051, 1033 and CQ. The Declarant demonstrates, however, that even when experiments are conducted at different times, the values of CC are consistent and very reproducible when tested at 10  $\mu$ m, which is the standard concentration of the test compounds used in the ionophore test. "Since the values obtained for both the positive

control (CQ) and negative control (metal alone) were consistent and reproducible at such low concentrations in the ionophore test", the Declarant was "confident that the values relating to the amount of copper uptake by compounds 1051, 1033 and CQ in the ionophore test...would also be consistent and reproducible, whether CC were tested side by side with the other test compounds or at a different time to 1051 and 1033" (See Paragraphs 17 and 18 of second Declaration). Thus, the Declarant concluded that this data together with the data obtained when comparing the values of 1051 and CC show that 1051, and especially 1033, are superior ionophores to the prior art compound CC.

This conclusion is further confirmed in the second Declaration when a contemporaneous side by side comparison of CQ, CC, 1051 and 1033 was performed in the ionophore test.

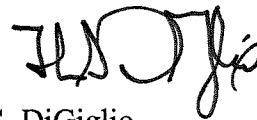
The results of the contemporaneous side by side experiments in the ionophore test are provided in Paragraph 23 of the second Declaration, which demonstrate that the value of copper uptake in the presence of CC was 1.32  $\mu\text{M}$ , while the value for copper uptake in the presence of 10  $\mu\text{M}$  of 1051 was 1.74  $\mu\text{M}$ , the value for copper uptake for CQ was 0.51  $\mu\text{M}$ , and the value of copper uptake in the presence of 2  $\mu\text{M}$  1033 was 1.51  $\mu\text{M}$ . As testified by Dr. Cherny, the data "confirm that 1033 is a far superior ionophore to CC" and "that 1051 is clearly a superior ionophore to CC". (See Paragraph 24 of second Declaration.)

Declarant concludes that both 1033 and 1051 are expected to be significantly more effective in reducing the levels of Abeta, a common target of Alzheimer's disease therapies, relative to CC (see Paragraphs 24 and 26 of second Declaration). Based on the testimony of Dr. Cherny and the data presented in the first and second Declarations, it is respectfully submitted that both 1051 and 1033 represent a patentable departure over the CC compound of the prior art.

With respect to the '112 issue, Claims 37, 39 and 41 have been cancelled, thereby rendering moot the rejection thereof.

Thus, in view of the amendment to the claims, the second Declaration of Dr. Cherny and the Remarks herein, it is respectfully submitted that the present case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'F. S. DiGiglio', with a stylized flourish at the end.

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